

SUBSTITUTE FORM PTO-1390

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTORNEY'S DOCKET NUMBER
08291-435001**TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371**

U.S. APPLICATION NO. (IF KNOWN)

09/509308INTERNATIONAL APPLICATION NO.
PCT/GB98/02863INTERNATIONAL FILING DATE
September 22, 1998PRIORITY DATE CLAIMED
September 25, 1997

TITLE OF INVENTION

DEACTIVANTS FOR DUST MITE ALLERGENS

APPLICANT(S) FOR DO/EO/US

Janette SUH, Malcolm Tom McKECHNIE, Gay CORNELIUS and Ian Andrew THOMPSON

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☒ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made.
8. ☐ A translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)) (UNSIGNED).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other documents or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:
 - ☒ Copy of PCT Written Opinion dated 16 August 1999
 - ☒ Copy of International Preliminary Examination Report dated 17 December 1999
 - ☐
 - ☐
 - ☐
 - ☐

"EXPRESS MAIL" Mailing Label Number


EE6471.86485US

Date of Deposit

March 23, 2000

I hereby certify under 37 CFR 1.10 that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office To Addressee" with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Valentin Figueroa
Valentin Figueroa

U.S. APPLICATION NO. (IF KNOWN) 09/309308		INTERNATIONAL APPLICATION NO. PCT/GB98/02863		ATTORNEY'S DOCKET NUMBER 08291-435001	
17. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):					
Search report has been prepared by the EPO or JPO..... \$840				\$0.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482) .. \$670				\$0.00	
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)).... \$690				\$0.00	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$970				\$970.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2) to (4) \$96				\$0.00	
ENTER APPROPRIATE BASIC FEE AMOUNT				\$970.00	
Surcharge of \$130 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 mos. from the earliest claimed priority date (37 CFR 1.492(e)).				\$0.00	
Claims	Number Filed	Number Extra	Rate		
Total Claims	16 - 20		x \$18	\$0.00	
Independent Claims	5- 3	2	x \$78	\$156.00	
Multiple Dependent Claims(s) (if applicable)			+ \$260	\$0.00	
TOTAL OF ABOVE CALCULATIONS				\$1,126.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28.)				\$0.00	
SUBTOTAL				\$1,126.00	
Processing fee of \$130 for furnishing the English Translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 mos. from the earliest claimed priority date (37 CFR 1.492(f))				\$0.00	
TOTAL NATIONAL FEE				\$1,126.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31).				\$0.00	
TOTAL FEES ENCLOSED				\$1,126.00	
				Amount to be refunded	
				Charged	
<p>a. <input checked="" type="checkbox"/> A check in the amount of \$1,126.00 to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. 06-1050 in the amount of \$0.00 to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1050. A duplicate copy of this sheet is enclosed.</p>					
<p>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.</p>					
SEND ALL CORRESPONDENCE TO:					
Frederick H. Rabin FISH & RICHARDSON P.C. 45 Rockefeller Plaza, Suite 2800 New York, NY 10111 (212) 765-5070 phone (212) 258-2291 facsimile			 SIGNATURE		
			Frederick H. Rabin NAME		
Date: <u>23 March 2000</u>			24,488 REGISTRATION NUMBER		

09/509308

Attorney's Docket No.: 08291-435001 / 10184P1-US

430 Rec'd PCT/PTO 23 MAR 2000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Janette SUH et al.
Serial No. : PCT/GB98/02863
Filed : 22 September 1998
Title : DEACTIVANTS FOR DUST MITE ALLERGENS

BOX: PCT

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the Specification:

Page 1, after the title: insert, as a heading

--Background of the Invention--.

Page 2, after line 20: insert, as a heading:

--Disclosure of the Invention--.

In the Claims:

Claim 6, line 30 (counting each structural formula as one line): delete "xxi) urea,".

Claim 7, line 1, change "claims 1, 2, 4 or 5" to --claim 1--.

Claim 10, line 27 (counting each structural formula as one line): delete "xxi) urea,".

CERTIFICATE OF MAILING BY EXPRESS MAIL

Express Mail Label No EE647186485US

I hereby certify under 37 CFR §1.10 that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to the Assistant Commissioner for Patents, Washington, D C 20231

Date of Deposit March 23, 2000

Signature Valentin Figueroa

Typed or Printed Name of Person Signing Certificate Valentin Figueroa

Claim 11, line 1: change “claims 8 or 9” to --claim 8--.

Claim 12, line 1: change “claims 8 to 11” to --claim 8--.

Claim 13, line 1: change “claims 8 to 12” to --claim 8--.

Claim 14, line 1: change “claims 8 to 13” to --claim 8--.

Claim 16, line 1: change “claims 8 to 15” to --claim 8--; same claim, line 4: change “fragramce” to --fragrance--.

In the Abstract:


Please insert the following pages 43-44 into the application.

REMARKS

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 23 March 00


Frederick H. Rabin
Reg. No. 24,488

Fish & Richardson P.C.
45 Rockefeller Plaza, Suite 2800
New York, NY 10111
Telephone: (212) 765-5070
Facsimile: (212) 258-2291

Deactivants for Dust Mite Allergens

It has been known for a long time that house dust can trigger allergenic reactions in humans, such as asthma and rhinitis. It was reported, as early as 1928, that it was the dust mites in the dust that were the primary source of the allergenic response but it was only in the 1960's that researchers appreciated its significance.

It is believed that the faeces of two particular house dust mite species, *Dermatophagoides farinae* (known as Der-f) and *Dermatophagoides pteronyssinus* (known as Der-p) trigger the immune responses of the body, thereby giving rise to well known allergenic symptoms.

A review of this is given in Experimental and Applied Acarology, 10 (1991) p. 167-186 in an article entitled "House dust-mite allergen" : A review by L. G. Arlian.

Both the Der-f and Der-p species are found throughout the world. In some areas, Der-f will be the sole *Dermatophagoides* species. In other areas Der-p will be the sole species. In still other areas, the two species are both present through, generally, one or the other will predominate.

One way to overcome these allergenic response has been to vacuum surfaces, such as carpets, that contain the dust mites and their faeces thoroughly and often, but that is both time consuming (i.e. has to be regularly done if one wants to make an allergenic free environment) and is very dependant on the efficiency of vacuum cleaner and filter bag used e.g. micron filter bag or 2-layer vacuum bags.

An alternative method of creating an allergen-free environment has been to denature the allergen, for example as described in US Patent No. 4,806,526. The only effective method however of which we are aware is to
5 apply tannic acid to the allergen. However, tannic acid can cause staining, and this is a particularly acute problem for light coloured carpets (e.g. white and light beige carpets) and other textile surfaces as tannic acid leaves a deep brown stain.

10 Therefore, we have been looking for allergenic denaturants which will not stain susceptible surfaces such as carpets and still deactivate the allergen.

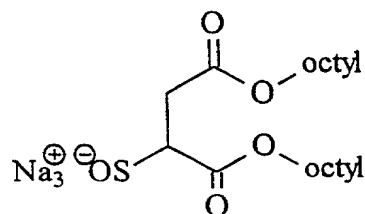
We have discovered a number of allergen deactivants which are effective against both the Der-f and the Der-
15 p species. Quite surprisingly, we have discovered that some of these deactivants are specific to the type of dust mite allergen being treated. For example an effective Der-f allergen deactivants will not automatically work effectively as a Der-p allergen
20 deactivant.

According to the invention there is provided a method for deactivating allergens derived from the Der-f and/or Der-p dust mite species, which comprises contacting the allergen with a deactivating effective
25 amount of one or more of deactivants (herein after defined as the deactivant).

The deactivants effective against one or both of Der-f allergens and Der-p allergens are:

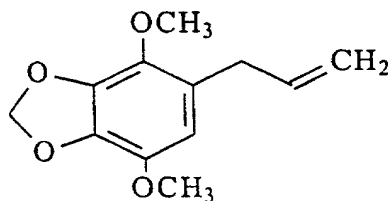
- i) cedarwood oil,
- 30 ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10

- vi) silica gel,
 vii) propylene glycol alginate,
 viii) ammonium sulphate,
 ix) hinokitiol,
 5 x) L-ascorbic acid,
 xi) "immobilised tannic acid", (hereinafter defined)
 xii) chlorohexidine,
 xiii) maleic anhydride,
 10 xiv) hinoki oil,
 xv) a composite of AgCl and TiO₂,
 xvi) diazolidinyl urea,
 xvii) 6-isopropyl-m-cresol,
 xviii) a compound of formula I

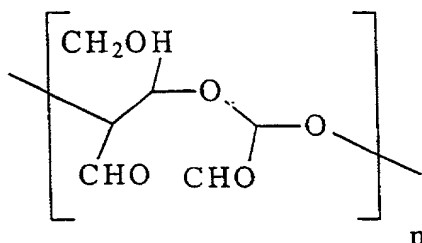


15

- xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



5 where $n = 2$ to 200,

- xxi) urea,
 xxii) cyclodextrin,
 xxiii) hydrogenated hop oil,
 xxiv) polyvinylpyrrolidone,
 10 xxv) N-methylpyrrolidone,
 xxvi) the sodium salt of anthraquinone,
 xxvii) potassium thioglycolate, and
 xxviii) glutaraldehyde

Deactivants (i) through (xx) are effective against both
 15 Der-f and Der-p allergens. Deactivants (xxi) through (xxvi) are effective against Der-f allergens only. Deactivants (xxvii) and (xxviii) are effective against Der-p allergens only.

A compound of formula I is commercially available as
 20 Aerosol OT.

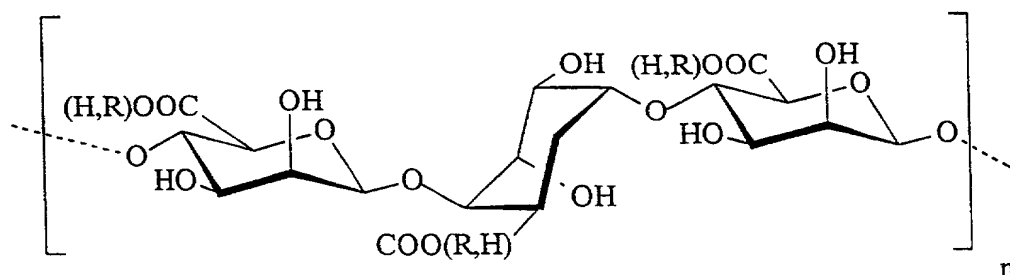
The compound of formula II is commercially available as parsley camphor.

Hinoki oil is a mixture of thujan-3-one, 2-pinene, 3,5,7,3',4'-pentahydroflavanone and 1,3,3-trimethyl-2-
 25 norcamphanone.

Hydrogenated Hop Oil is the potassium salt of tetrahydroiso humulinic acid (also known as reduced isomerised hop extract).

Propylene glycol alginate is

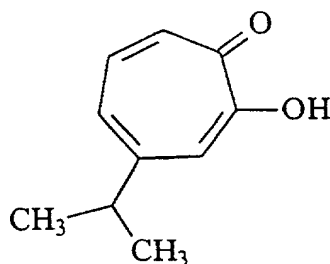
5



Chlorohexadine is 1,1'-hexamethylenebis[5-(4-chlorophenyl)]-biguanide.

Hinokitol is β -thujaplicin, a compound of the formula

10



Germall II is diazolidinylurea.

Thymol is 6-isopropyl-m-cresol.

Cedarwood oil contains α - and β -cedrene (ca 80%), cedrol (3-14%) and cedrenol. Other sesquiterpenes and some monoterpenes are also present.

15

Polyquaternium-10 is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with a trimethyl ammonium substituted epoxide commercially available as Polymer JR-125.

5 Silica gel is also known as colloidal silica or silicic acid and is commercially available as Kent.

 "Immobilised tannic acid" is tannic acid on polyvinyl pyrrolidone beads. Immobilised Tannic Acid was prepared as follows: 100 mg of tannic acid was dissolved
10 in water; 50 mg of Polyclar 10 (ISP, Guildford Surrey) polyvinyl pyrrolidone beads were added and stirred for one hour; the beads were filtered off the solution and washed with a few mls of iced water until no colour was seen in the washings; they were then dried in the oven at
15 50°C.

 The composite of silver chloride and TiO_2 is made up of 20% wt/wt AgCl on 80% TiO_2 3-5 μm porous beads.

 In compositions containing the deactivant, the deactivant is present in an amount of from 0.01% to 7%,
20 preferably from 0.01% to 3%.

 In methods for treating rugs and carpets to deactivate allergents, the amount of deactivant present is from about 16gm to about 170gm per 10 square meters, preferably about 32gm per 10 square meters.

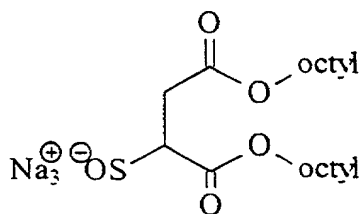
25 Preferably the deactivant is selected from

- xiv) hinoki oil,
- xv) a composite of AgCl and TiO_2 ,
- xvi) diazolidinyl urea
- xvii) 6-isopropyl-m-cresol,
- 30 xii) chlorohexidine,
- xiii) maleic anhydride,

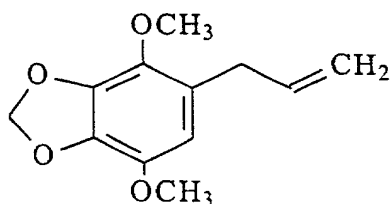
- xxvi) the sodium salt of anthraquinone and
- xviii) a compound of formula I or II, defined above, and
- xix) a compound of formula II, defined above.

5 Further according to the invention there is provided an aerosol composition containing

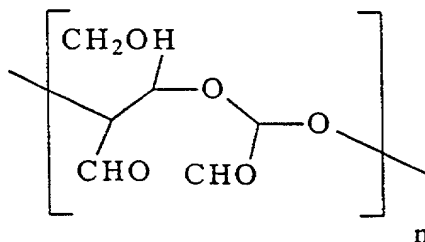
- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- 10 iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- 15 ix) hinokitiol,
- x) L-ascorbic acid,
- xi) "immobilised tannic acid", (hereinafter defined)
- xii) chlorohexidine,
- 20 xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂.
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- 25 xviii) a compound of formula I



xix) the compound of formula II



xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



where $n = 2$ to 200,

- xxi) urea,
- xxii) cyclodextrin,
- 10 xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone,
- xxvi) the sodium salt of anthraquinone,
- xxvii) potassium thioglycolate, and
- 15 xxviii) glutaraldehyde

b) a propellant, and

c) optionally, a solvent.

Preferably the amount of deactivant present in such a composition is from 0.01% to 7%, more preferably 0.01% to 3%,

Preferably the amount of propellant present in such a composition is from 4% to 50%, more preferably from 4% to 30%,

Preferably the amount of solvent present in such a composition is 0% to 99.95%, more preferably 0% to 90%, and most preferably from 20% to 90%.

10 Preferably the deactivant in such aerosol composition is selected from

hinoki oil,
a composite of AgCl with TiO_2 ,
diazolidinyl urea,
15 6-isopropyl-m-cresol,
chlorohexidine,
maleic anhydride,
the sodium salt of anthraquinone, and
a compound of formula I or II defined above.

20 Preferably the propellant is selected from those commercially available, for example C_{1-4} alkanes, chlorofluorocarbons and compressed gases such as nitrogen, air and carbon dioxide.

Preferably the solvent is selected from C_{1-6} alcohols
25 (e.g. ethanol) or water.

In addition, the compositions of this invention may also contain one or more of the following:

a fragrance, preferably in an amount of 0% to 5%, more preferably 0% to 2%;

an antimicrobial compound e.g.
alkyldimethylbenzyl ammonium saccharinate,
preferably in an amount of 0.01% to 1%;

5 a surfactant, e.g. Dow Corning 193 Surfactant,
preferably in an amount of 0.01% to 1%;

a corrosion inhibitor, e.g. sodium nitrite,
sodium benzoate, triethanolamine and ammonium
hydroxide, preferably in an amount of 0.01% to 10%;
and

10 a miticide, such as benzyl benzoate, pyrethroid
permethrin, d-allethrin and optionally a synergist
such as piperonyl butoxide, preferably in an amount
of 0.1% to 10%.

It has been found that deactivants of the invention
15 have as effective allergen deactivating properties as
tannic acid but without the drawback of staining.

The invention will now be illustrated by the
following Examples.

Examples

20 The test procedure in Examples 1 to 55 is as follows
and is known as the ELISA protocol.

The ELISA protocol for Der-f and Der-p has been
developed as follows as a measure of denaturing property
for denaturants.

25 ELISA Protocol 1

1. Dust is collected from Hoover™ vacuum cleaner bags
and passed through a series of sieves down to 63 microns.

2. Clean petri dishes are labelled with the chemical to be tested (on the base). Three replicates are used for each treatment.
3. Filter paper is used to line each dish and 0.2g of dust is added to each dish onto the filter paper. The lid (or base, as dishes are inverted) is replaced and the dish is shaken to disperse the dust evenly over the filter paper.
4. 2% aqueous solutions of deactivant were used except for the silver chloride composite where 0.05% was used instead. Immobilised tannic acid was used as a 1% dispersion. The hydrogenerated hop end was used at the 2% level (in the form of a 10% solution). Water-insoluble deactivants were emulsified with a sorbitone oleate surfactant (i.e. Tween). Hinokitol was used at 0.5% not 2%.
5. The dust is sprayed with the corresponding treatment, 2 sprays are required for sufficient coverage (1 spray = 1.5 ml).
6. Leave uncovered at room temperature, in well aerated room, until filter paper is dry. This can take up to 4 hours.
7. Empty dust in epindorfs labelled according to treatment.
8. Add 1 ml of 5% Bovine Serum Albumen Phosphate Butter Saline - Tween BSA-PBS-T to each epindorf (5 times the weight of dust) (20ml of BSA-PBS-T = 1 g of BSA in 20ml of PBS-T).
9. Leave overnight in a refrigerator.
10. Centrifuge for 5 minutes at 13,000 rpm.

11. Decant the supernatant into a new epindorf labelled according to treatment.
12. Centrifuge again for 5 minutes at 13,000 rpm.
13. Make up dilutions of 1:10 and 1:100 by adding 100 μ l of neat solution to 900 μ l of 1% BSA-PBS-T (1:10). This is repeated using 100 μ l of 1:10 dilution and add to 900 μ l of 1% BSA-PBS-T for 1:100 dilution.

ELISA Protocol 2 for Der-f and Der-p: Indoor Biotechnologies

- 10 1. Prepare samples and dilutions as in protocol
2. Prepare 500 ml of 50 mM carbonate/bicarbonate buffer by dissolving 0.795g Na_2CO_3 and 1.465g NaHCO_3 in 500 ml of distilled water. Check the pH is at 9.6. (This solution is kept in the refrigerator in a conical flask).
- 15 3. Monoclonal antibody (kept in the freezer) has to be added to the buffer using the following method, (1 μ g per well; 11 ml is needed) applied to the ELISA plate
 - 11ml of carbonate/bicarbonate buffer is added to the dispensing tray.
 - 20 - 11 μ l of Der-f1 or Der-p1 monoclonal antibody
- (Stored in freezer, epindorf in use is in the refrigerator) is added to the buffer. To ensure that all the antibody is removed from the tip, wash out the pipette tip by sucking up and down I the buffer solution,
- 25 gently stirring to mix thoroughly.
4. Pipette 100 μ l of the antibody solution into each well of the microtiter plate, cover with a plate sealer and leave overnight at 4°C.

5. Empty the plate by quickly inverting it over the sink, then dry by banging on a stack of paper towels.
6. Add 200 µl of wash buffer to each well: PBS/0/05% tween (PBS-T).
- 5 7. Repeat stages 5 and 6 once more (making a total of 2 washes).
8. Make sure all the wells are dry, then add 100 µl of 1% BSA-PBS-T. Replace the plate sealer and incubate for 1 hour at room temperature*.
- 10 9. Repeat steps 5 to 7 (2 washes).
10. *During the hour incubation period, prepare the allergen standards at dilutions between 125 and 1 µg/ml Der f 1 or Der p1:
- 15 - Add 25 µl of allergen standard (kept in the refrigerator in polystyrene box) to 475 µl of 1% PBS-BSA-T and mix thoroughly - labelled '125'.
 - 250 µl of 1% PBS-BSA-T is added to 7 further epindorfs which are labelled 62.5, 31.25, 15.63, 7.61, 3.9, 1.95 and 0.98.
 - 20 - 250 µl is taken from the 1st epindorf (labelled 125) and transferred to the next (labelled 62.5). This is mixed thoroughly.
 - Using a new pipette tip, 250 µl is removed from epindorf labelled 62.5 and transferred to 31.25,
 - 25 this procedure is continued down to the 0.98 concentration (125, 62.5, 31.25, 15.63, 7.61, 3.9, 1.95, 0.98)
 - In total $475 + (250 \times 7) = 2.3\text{ml}$: 0.023g of BSA added to 2.3 ml of PBS-T.

11. Add 100µl aliquots of the allergen sample to the plate along with the standard allergen samples for the reference curve in duplicate. The standards usually go in the first two columns on the left hand side, with the least concentrated on top. Incubate for 1 hour.
12. Follow stages 5 to 6, completing a total of 5 washes.
13. Pour 11 ml of 1% BSA-PBS-T (0.11g of BSA to 11ml of PBS-T) to the dispensing tray. Add 11 µl of the biotinylated monoclonal antibody (refrigerator) and mix thoroughly.
14. Pipette 100 µl into each well and incubate for 1 hour at room temperature.
15. Empty plate and wash as described in stage 12. (5 washes).
16. Add 11 µl of Streptavidin (freezer) to 11 ml of 1% BSA-PBS-T. Pipette 100 µl into each well and incubate for 30 minutes. Reserve any remaining solution in a vial.
17. Empty plate and wash as described in stage 12 (5 washes).
18. Make a solution of OPD, by putting the two tablets (in silver and gold foil) into 20 ml of distilled water (in a glass vial). Shake quite vigorously in the dark until the tablets have dissolved (Wrap the vial up either in tin foil or paper towel).
19. Add a small amount to the remaining solution from stage 16. Wait for a colour change (positive reaction). Add 200 µl to each well and incubate for a minimum of 30 minutes in the dark.

20. Read the plate at 450nm/405nm if filter not available.

Examples 1 to 26

The deactivants, as set out in the following table,
5 were used against Der-f allergens according to the above procedure and the results are as given below. Tannic acid was used as a comparator. What was measured after treatment with deactivant and tannic acid was the amount of allergen remaining active after treatment. The ratio
10 of amount of remaining active allergen after treatment with deactivant and tannic acid is also given.

Table

Example	Deactivant	Amount of Allergen remaining active after deactivant treatment	Amount of Allergen remaining active after tannic acid treatment	Ratio of remaining active allergen after Deactivant/Tannic Acid Treatment	Number
1	Urea	3750	1500	2.500	xxi
2	Polymetric dialdehyde	1325	550	2.409	xx
3	Cedarwood oil	1800	750	2.400	i
4	Cyclodextrin	3850	1700	2.265	xxii
5	hexadecyltrimethylammonium chloride	4075	1800	2.264	ii
6	Aluminium chlorohydrate	1675	750	2.233	iii
7	1-propoxy-propanol-2	3950	1800	2.194	iv
8	Silica Gel (Kent)	2037.5	933.5	2.183	vi
9	polyquaternium-10 (Polymer JR-125)	4335	2000	2.168	v
10	Hydrogenated Hop Oil	1100	550	2.000	xxiii
11	Propylene glycol alginate	3175	1700	1.868	vii
12	Poly vinyl pyrrolidone	2450	1425	1.719	xxiv
13	Ammonium sulphate	2750	1700	1.618	viii

Example	Deactivant	Amount of Allergen remaining active after deactivant treatment	Amount of Allergen remaining active after tannic acid treatment	Ratio of remaining active allergen after Deactivant/Tannic Acid Treatment	Number
14	Hinokitol (0.5%)	3065	2000	1.533	ix
15	N-methyl pyrrolidone	1600	1175	1.362	xxv
16	L-Ascorbic Acid	2000	1500	1.333	x
17	Immobilised Tannic Acid	1550	1175	1.319	xi
18	Aerosol OT	1525	1175	1.298	xviii
19	Chlorohexidine	1412.5	1425	0.991	xii
20	Parsley Camphor	1225	1387.5	0.883	xix
21	Maleic anhydride	1312.5	1500	0.875	xiii
22	Anthraquinone sodium salt	1530	2000	0.765	xxvi
23	Hinoki oil	1025	1387.5	0.739	xiv
24	Composite of AgCl and TiO ₂	1025	1425	0.719	xv
25	Germall II	950	1387.5	0.685	xvi
26	Thymol	725	1387.5	0.523	xvii

Examples 27 to 47

The deactivants, as set out in the following table, were used against Der-p allergens according to the above procedure and the results are as given below. What was
5 measured were the amount of allergens remaining after treatment with deactivant and the amount of allergens remaining after vacuuming with no deactivant treatment.

Table

Example	Deactivant	Amount of active Allergen remaining after deactivant treatment	Amount of active Allergen remaining after no deactivant treatment but only vaccuming	Deactivant
1	Glutaraldehyde	816	3375	xxviii
2	Polymetric dialdehyde	2792	3375	xx
3	Cedarwood oil	3375	6000	i
4	hexadecyltrimethylammonium chloride	2863	4992	ii
5	Aluminium chlorohydrate	978	4992	iii
6	1-propoxy-propanol-2	1233	4992	iv
7	Silica Gel (Kent)	1540	4992	vi
8	polyquaternium-10 (Polymer JR-125)	5463	6250	v
9	Propylene glycol alginate	3781	6250	vii
10	Ammonium sulphate	2325	6250	viii
11	Potassium thioglycolate	3092	3375	xxvii

Example	Deactivant	Amount of active Allergen remaining after deactivant treatment	Amount of Allergen remaining after no deactivant treatment	Deactivant
12	Hinokitol (0.5%)	2058	3375	ix
13	L-Ascorbic Acid	1438	5642	x
14	Immobilised Tannic Acid	1125	5642	xi
15	Aerosol OT	4494	5642	xviii
16	Chlorohexidine	2281	4450	xii
17	Parsley Camphor	2581	4450	xix
18	Maleic anhydride	783	4450	xiii
19	Hinoki oil	1644	3400	xiv
20	Composite of AgCl and TiO ₂	1632	3400	xv
21	Thymol	1500	3400	xvii

Examples 48-55

Further samples were tested as above and compared against tannic acid. The ratio of actives remaining after deactivant treatment and actives remaining after tannic acid treatment are given below:

Example	Deactivant	Ratio of actives remaining after deactivant treatment over those remaining after tannic acid treatment	Number
48	Germall II	1.5	vi
49	N-methyl pyrrolidone	4.0	xv
50	Hinoki Oil	4.0	iv
51	Silver chloride/TiO ₂	3.5	v
52	Thymol	4.0	vii
53	Chlorohexidine	3.0	ii
54	Maleic anhydride	1.0	iii
55	Glutaraldehyde	1.5	xviii

Examples 56-59

The following formulations can be made up as carrier compositions for use in an aerosol for deactivating Der-f and Der-p allergens.

Example 56

<u>Raw Ingredient Description</u> <u>By Weight</u>	<u>Item Classification</u>	<u>%</u>
Anhydrous Ethanol (SD Alcohol 40)	Solvent	79.646
Alkyl dimethyl benzyl ammonium saccharinate	Cationic Surfactant	0.106
Corrosion Inhibitor (I)		0.192
Corrosion Inhibitor (II)		0.192
Corrosion Inhibitor (III)		0.096
Deionized Water	Water/Solvent	15.768
Carbon Dioxide	Propellant	4.000
TOTAL		100.000

Example 57

<u>Raw Ingredient</u> <u>Description by Weight</u>	<u>Item Classification</u>	<u>%</u>
Anhydrous Ethanol (SD Alcohol 40)	Solvent	* 57.000
Fragrance#17	Fragrance	0.0500
Dow Corning 193 Surfactant	Surfactant	0.025
Corrosion Inhibitor (I)		0.100
Corrosion Inhibitor (II)		0.100
Deionized Water	Water/solvent	* 14.725
NP-40/Butane 40	Hydrocarbon propellant	28.000
TOTAL		100.000

* = May replace with 95% Ethanol (SD Alcohol 40) at 61.755% by weight and 9.970% by weight Deionized water

Example 58

<u>Raw Ingredient</u> <u>Description by Weight</u>	<u>Item Classification</u>	<u>%</u>
Anhydrous Ethanol (SD Alcohol 40)	Solvent	79.646
Benzyl Benzoate - an acaricide	Active/ester	4.600
Alkyl dimethyl benzyl ammonium saccharinate	Cationic Surfactant	0.106
Corrosion Inhibitor (I)		0.192
Corrosion Inhibitor (II)		0.192
Corrosion Inhibitor (III)		0.096
Deionized Water	Water/solvent	11.168
Carbon Dioxide	Propellant	4.000
TOTAL		100.000

Example 59

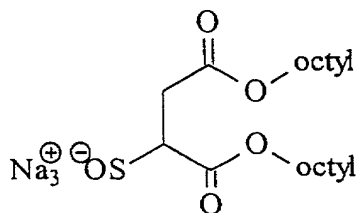
<u>Raw Ingredient</u> <u>Description by weight</u>	<u>Item Classification</u>	<u>%</u>
Anhydrous Ethanol (SD Alcohol 40)	Solvent	*57.000
Benzyl Benzoate	Active/ester	4.600
Fragrance#17	Fragrance	0.0500
Dow Corning 193 Surfactant	Surfactant	0.025
Corrosion Inhibitor (I)		0.100
Corrosion Inhibitor (II)		0.100
Deionized Water	Water/solvent	*10.125
NP-40/Butane 40	Hydrocarbon propellant	28.000
TOTAL		100.000

* = May replace 95% Ethanol (SD Alcohol 40) at 61.755% by weight and 5.370% by weight Deionized water.

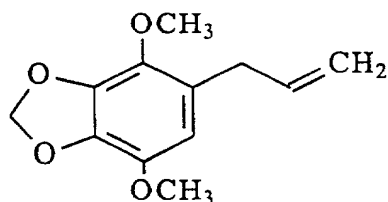
CLAIMS

1. A method for deactivating a Der-f and/or a Der-p allergen comprising contacting the allergen with a deactivating effective amount of one or more of deactivants selected from

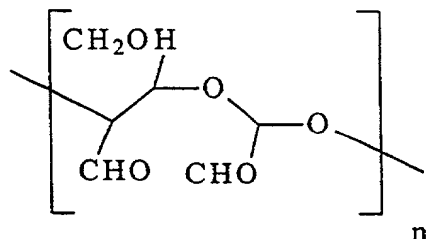
- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



xix) the compound of formula II



xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



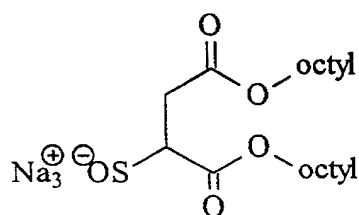
where $n = 2$ to 200,

- xxi) urea,
- xxii) cyclodextrin,
- xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone,
- xxvi) the sodium salt of anthraquinone,
- xxvii) potassium thioglycolate, and
- xxviii) glutaraldehyde.

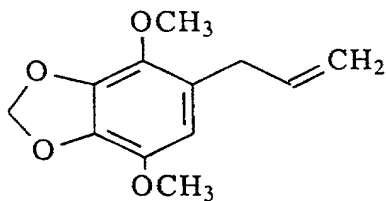
2. A method for deactivating a Der-f allergen comprising contacting the allergen with a deactivating effective amount of one or more deactivants selected from

- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,

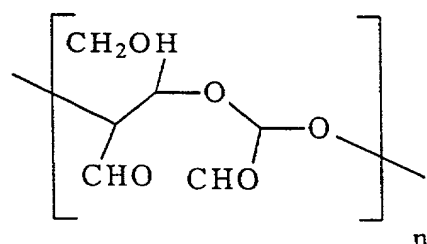
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



- xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



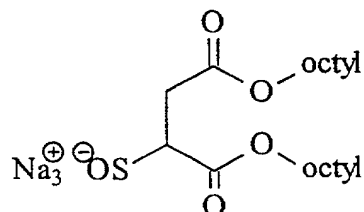
where $n = 2$ to 200 ,

- xxi) urea,
- xxii) cyclodextrin,
- xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone, and
- xxvi) the sodium salt of anthraquinone.

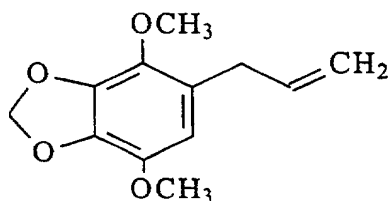
3. A method for deactivating a Der-p allergen comprising contacting the allergen with a deactivating effective amount of one or more deactivants selected from

- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,

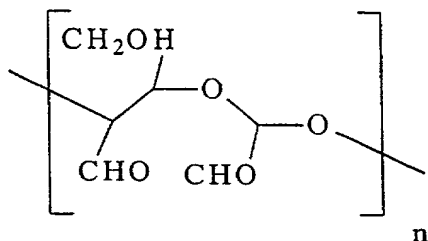
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



- xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III

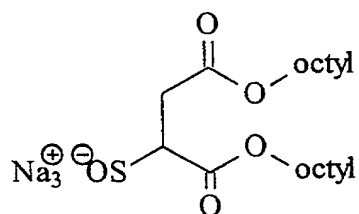


where n = 2 to 200,

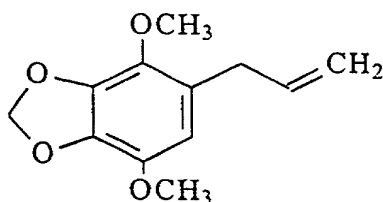
- xxvii) potassium thioglycolate, and
- xxviii) glutaraldehyde.

4. A method for deactivating allergens deriving from Der-f and/or Der-p dust mites, said allergens being associated with faecal particles excreted by said mites on the surfaces of fabric materials selected from rugs, carpet and upholstered furniture, which method comprises applying to said fabric materials a deactivant selected from

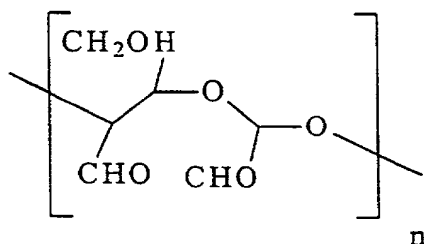
- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



xix) the compound of formula II



xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



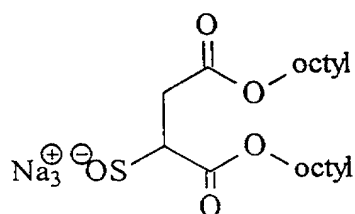
where $n = 2$ to 200,

- xxi) urea,
- xxii) cyclodextrin,
- xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone,
- xxvi) the sodium salt of anthraquinone,
- xxvii) potassium thioglycolate, and
- xxviii) glutaraldehyde

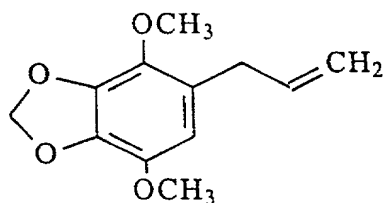
at an application rate of from 16 grams to 170 grams of deactivant per 10 square meters.

5. A method according to claim 4 in which the allergens derive from Der-f dust mites and the deactivant is selected from

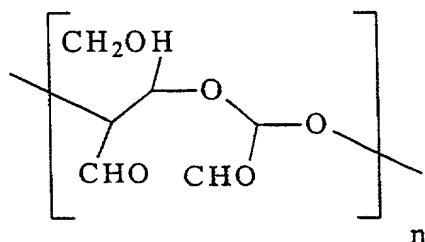
- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



- xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



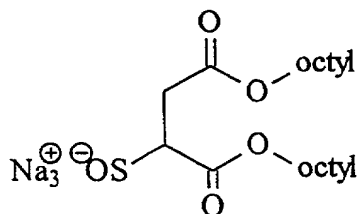
where $n = 2$ to 200,

- xxi) urea,
- xxii) cyclodextrin,
- xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone, and
- xxvi) the sodium salt of anthraquinone.

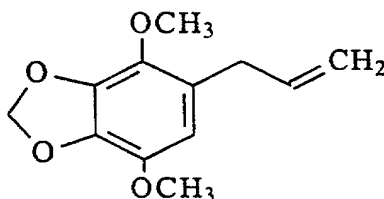
6. A method according to claim 4 in which the allergens derive from Der-p dust mites and the deactivant is selected from

- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,

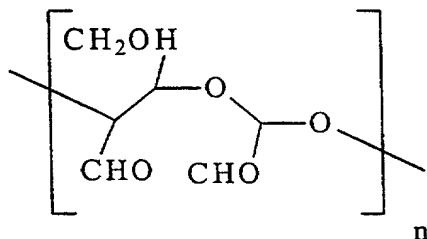
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



- xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



where n = 2 to 200,

- xxi) urea,
- xxvii) potassium thioglycolate, and
- xxviii) glutaraldehyde.

7. A method according to any of claims 1, 2, 4 or 5 in which the deactivant is selected from

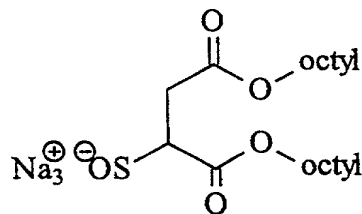
- xiv) hinoki oil,
- xv) a composite of AgCl with TiO₂,
- xvi) diazolidinyl urea
- xvii) 6-isopropyl-m-cresol,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xxvi) the sodium salt of anthraquinone,
- xviii) a compound of formula I, and
- xix) the compound of formula II.

8. An aerosol composition containing

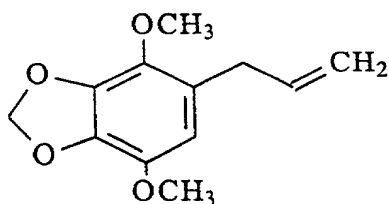
a) a deactivant selected from

- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,

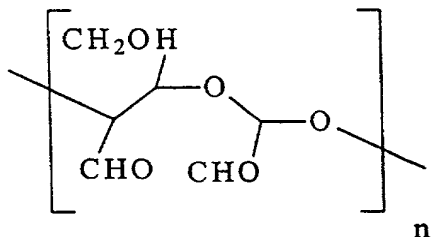
xviii) a compound of formula I



xix) the compound of formula II



xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III

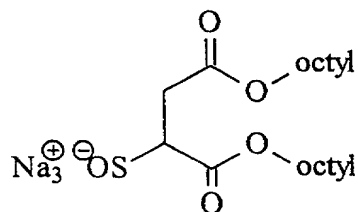


where $n = 2$ to 200,

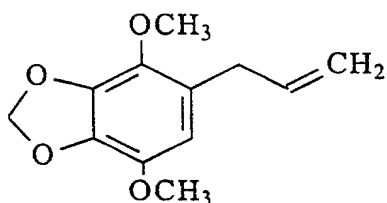
- xxi) urea,
- xxii) cyclodextrin,
- xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone,
- xxvi) the sodium salt of anthraquinone,
- xxvii) potassium thioglycolate, and

- xxviii) glutaraldehyde;
- b) a propellant; and
- c) optionally, a solvent.
9. An aerosol composition according to claim 8 in which the deactivant is selected from

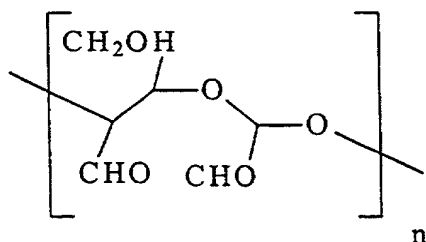
- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



xix) the compound of formula II



xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



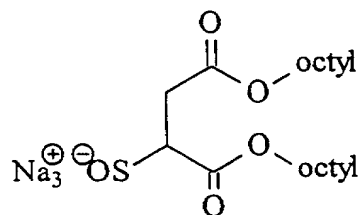
where $n = 2$ to 200,

- xxi) urea,
- xxii) cyclodextrin,
- xxiii) hydrogenated hop oil,
- xxiv) polyvinylpyrrolidone,
- xxv) N-methylpyrrolidone, and
- xxvi) the sodium salt of anthraquinone.

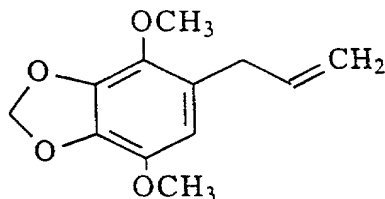
10. An aerosol composition according to claim 8 in which the deactivant is selected from

- i) cedarwood oil,
- ii) hexadecyltrimethylammonium chloride,
- iii) aluminium chlorohydrate,
- iv) 1-propoxy-propanol-2,
- v) polyquaternium-10

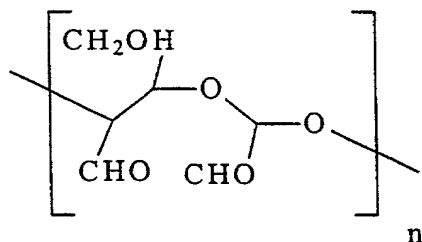
- vi) silica gel,
- vii) propylene glycol alginate,
- viii) ammonium sulphate,
- ix) hinokitiol,
- x) L-ascorbic acid,
- xi) immobilised tannic acid,
- xii) chlorohexidine,
- xiii) maleic anhydride,
- xiv) hinoki oil,
- xv) a composite of AgCl and TiO₂,
- xvi) diazolidinyl urea,
- xvii) 6-isopropyl-m-cresol,
- xviii) a compound of formula I



- xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



where $n = 2$ to 200 ,

- xxi) urea,
 xxvii) potassium thioglycolate, and
 xxviii) glutaraldehyde.
11. A composition according to claims 8 or 9 in which the deactivant is selected from

- xiv) hinoki oil,
 xv) a composite of AgCl with TiO_2 ,
 xvi) diazolidinyl urea
 xvii) 6-isopropyl-m-cresol,
 xii) chlorohexidine,
 xiii) maleic anhydride,
 xxvi) the sodium salt of anthraquinone,
 xviii) a compound of formula I, and
 xix) the compound of formula II.

12. A composition according to any of claims 8 to 11 in which the amount of deactivant present is from 0.01% to 7%, the amount of propellant present is from 0.05% to 3%, and the amount of solvent present is from 0% to 99.95%, all percentages being by weight.

13. A composition according to any one of claims 8 to 12 in which the propellant is selected from C_{1-4} alkane and carbon dioxide.

14. A composition according to any one of claims 8 to 13 in which the solvent is selected from C_{1-6} alcohols or water.

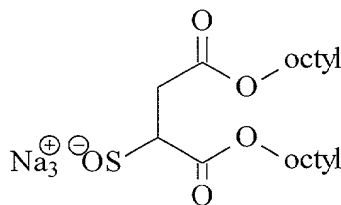
15. A composition according to claim 14 in which the solvent is ethanol.

16. A composition according to any one of claims 8 to 15 in which the composition may also contain one or more of the following:

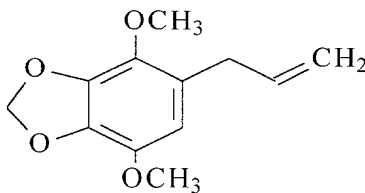
- a fragramce.
- a surfactant,
- an antimicrobial agent,
- a corrosion inhibitor, and/or
- a miticide.

Abstract of the Disclosure

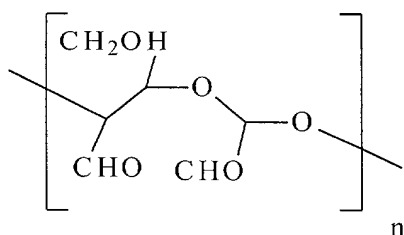
- Der-f and/or Der-p dust mite allergens are deactivated by an amount of one or more of the following deactivants: i) cedarwood oil, ii) hexadecyltrimethylammonium chloride, iii) aluminium chlorohydrate, iv) 1-propoxy-propanol-2, v) polyquaternium-10 vi) silica gel, vii) propylene glycol alginate, viii) ammonium sulphate, ix) hinokitiol, x) L-ascorbic acid, xi) immobilised tannic acid, xii) chlorohexidine, xiii) maleic anhydride, xiv) hinoki oil, xv) a composite of AgCl and TiO₂, xvi) diazolidinyl urea, xvii) 6-isopropyl-m-cresol, xviii) a compound of formula I



- 10 xix) the compound of formula II



- xx) a polymeric dialdehyde containing two or more of a recurring unit of the formula III



- where n = 2 to 200, xxi) urea, xxii) cyclodextrin, xxiii) hydrogenated hop oil, xxiv) polyvinylpyrrolidone, xxv) N-methylpyrrolidone, xxvi) the sodium salt of anthraquinone, xxvii) potassium thioglycolate, and xxviii) glutaraldehyde.
- 15 Deactivants (i) to (xx) are effective against allergens derived from both species. Deactivants (xxi) to (xxvi) are effective against only Der-f allergens. Deactivants (xxvii) and (xxviii) are effective against only Der-p allergens. Aerosol compositions comprise said deactivants, a propellant and optional solvents.

30012709.doc

COMBINED DECLARATION AND POWER OF ATTORNEY FOR UTILITY PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled
Deactivants for Dust Mite Allergens

the specification of which

☐ is attached hereto.

☐ was filed on _____ as Application Serial No. _____ and was amended on _____.

☒ was described and claimed in PCT International Application No. PCT/GB98/02863 filed on 22 September 1998 and was amended under PCT Article 19 on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with 37 C.F.R. § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119 of any foreign application(s) for patent or inventor's certificate or of any PCT International application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

COUNTRY	APPLICATION NO.	FILING DATE	PRIORITY CLAIMED
GB	9720275.8	25 September 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
GB	9720298.0	25 September 1997	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) or under 35 U.S.C. § 365(c) of any PCT International application designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose all information I know to be material to patentability as defined in 37 C.F.R. § 1.56(a) which became available between the filing date of the prior application and the national or PCT International filing date of this application:

COMBINED DECLARATION AND POWER OF ATTORNEY (CONTINUED)

Full Name of Inventor: Malcolm Tom MCKECHNIE

Inventor's Signature: _____ Date: _____

Residence: Drifffield, UNITED KINGDOM

Citizen of: UNITED KINGDOM

Post Office Address: Spring Rise, 12a North Road, Drifffield, East Yorkshire,
YO25 9TF, UNITED KINGDOM

Full Name of Inventor: Ian Andrew THOMPSON

Inventor's Signature: *Ian Andrew Thompson* Date: 4th May, 2000

Residence: New South Wales, AUSTRALIA

Citizen of: AUSTRALIA

Post Office Address: 2 Blanford Street, Collaroy Plateau-2097, New South Wales,
AUSTRALIA

Full Name of Inventor: _____

Inventor's Signature: _____ Date: _____

Residence: _____

Citizen of: _____

Post Office Address: _____

Full Name of Inventor: _____

Inventor's Signature: _____ Date: _____

Residence: _____

Citizen of: _____

Post Office Address: _____

COMBINED DECLARATION AND POWER OF ATTORNEY (CONTINUED)

APPLICATION NO. _____ FILING DATE _____ U.S. PATENT STATUS
☐ Pending ☐ Issued ☐ Abandoned

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:
 Frederick H. Rabin, Reg. No. 24,488; Andrew N. Parfomak, Reg. No. 32,431; John B. Pegram, Reg. No. 25,198; William J. Hone, Reg. No. 26,739; Richard P. Ferrara, 30,632; Stephan J. Filipek, Reg. No. 33,384; and George E. Heibel, Reg. No. 42,648.

Address all telephone calls to Frederick H. Rabin at telephone number 212/765-5070.

Address all correspondence to Frederick H. Rabin, Fish & Richardson P.C., 45 Rockefeller Plaza, New York, NY 10111.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Full Name of Inventor: Janette SUH

Inventor's Signature: [Signature] Date: 5/4/2000

Residence: New Jersey, UNITED STATES

Citizen of: UNITED STATES

Post Office Address: Thomas Lane, Ho-Ho-Kus 07423
690 River Road, New Milford, New Jersey 07646, UNITED STATES

Full Name of Inventor: Gay CORNELIUS

Inventor's Signature: [Signature] Date: 18.5.00

Residence: Cottingham, UNITED KINGDOM

Citizen of: UNITED KINGDOM

Post Office Address: 57 The Wolds, Cottingham, East Yorkshire, HU16 5LQ,
UNITED KINGDOM

COMBINED DECLARATION AND POWER OF ATTORNEY (CONTINUED)

Full Name of Inventor: 300 Malcolm Tom MCKECHNIE

Inventor's Signature: Mald McKech

Date: 18th May 00

Residence: Drifffield, UNITED KINGDOM

Citizen of: UNITED KINGDOM

Post Office Address: Spring Rise, 12a North Road, Drifffield, East Yorkshire,
YO25 9TF, UNITED KINGDOM

Full Name of Inventor: 40 Ian Andrew THOMPSON

Inventor's Signature: _____

Date: _____

Residence: New South Wales, AUSTRALIA

Citizen of: AUSTRALIA

Post Office Address: 2 Blanford Street, Collaroy Plateau-2097, New South Wales,
AUSTRALIA

Full Name of Inventor: _____

Inventor's Signature: _____ Date: _____

Residence: _____

Citizen of: _____

Post Office Address: _____

Full Name of Inventor: _____

Inventor's Signature: _____ Date: _____

Residence: _____

Citizen of: _____

Post Office Address: _____